

Amendments to the Specification:

Please replace the paragraph starting on page 55, line 21 with the following rewritten paragraph:

-- The single target counting methods and assays described above may be adapted for use in detecting and quantitating target nucleic acid sequences or species in a sample (*e.g.*, DNA, RNA, *etc.*). As such, in one aspect, the present invention provides a method of detecting the presence of at least one target nucleic acid sequence in a sample, said method comprising: labeling at least one target nucleic acid sequence with at least one quantum dot; and detecting the labeled target nucleic acid sequence by detecting fluorescence emitted by the at least one quantum dot, wherein the detection of fluorescence in the sample indicates the presence of at least one target nucleic acid sequence. Preferably, the method further comprises quantitating the target nucleic acid sequence by analyzing the detected emitted fluorescence. In one preferred embodiment, the method further comprises transcribing the target nucleic acid sequence. In another preferred embodiment, the target nucleic acid sequence is DNA and transcribing comprises using a primer which anneals to a conserved region of the DNA and transcribes a polymorphic region of the DNA when extended. --

Please replace the paragraph starting on page 56, line 29 with the following rewritten paragraph:

-- Several different qualitative assays for detecting the presence of K-ras DNA circulating in human plasma have been reported in the literature. These methods generally involve PCR amplification of target, and include technologies such as, sequence specific hybridization, sequence specific PCR, SSCP, or TaqMan, RFLP or DNA sequencing. None of these methods report focused attempts at quantitating the level of K-ras target in the plasma. In general, assays involving target amplification are not desirable for quantitative assays, since the efficiency of the amplification step can vary dramatically between different samples. The assays of the present invention involve directly detecting and counting the target DNA from the patient sample, thus measuring the amount of K-ras DNA in the sample without an amplification step. This is accomplished with the use of individual or single molecules of quantum dots to detect each target molecule. --

Please replace the paragraph starting on page 57, line 6 with the following rewritten paragraph:

-- An *in vitro* assay has been designed accordingly. Specifically, the assay is designed to detect and quantitate a target species, in this case K-ras, in plasma. The assay has sufficient sensitivity to achieve this with very low levels of K-ras target. In addition, the assay is used to determine the genotype for 5-6 point mutations located in the K-ras DNA and to select mutant DNA away from the wild type. Typically, the wild type is the predominant sequence within the sample. --

Please replace the paragraph starting on page 57, line 12 with the following rewritten paragraph:

-- In this exemplary assay, synthetic or plasmid target containing 2-3 K-ras mutations (e.g. exon 12) and synthetic or plasmid target of wild type K-ras are used as the target species. Sequence information for the entire target and mutations should be known. A primer is designed which anneals to a conserved region, and when extended will transcribe the polymorphic region of K-ras. In this embodiment, 5' biotinylated oligonucleotide primers are used for simultaneously labeling and transcribing the target sequence. It will be readily apparent to those of skill in the art that the primer can be labeled with any immobilizable label or tag. A number of different immobilizable tags and capture moieties can be used that are based upon numerous molecular interactions well described in the literature. For instance, where an immobilizable tag has a natural binder (e.g., biotin, protein A or protein G), it can be used in conjunction with an appropriate capture moiety (e.g., avidin, streptavidin, neutravidin, the Fc region of an immunoglobulin, etc.). Moreover, antibodies to molecules having natural capture moieties, such as biotin, are also widely available as appropriate capture moiety or tag binders (see, SIGMA Immunochemicals 1998 catalogue, SIGMA Chemical Co. (St. Louis MO)). Conditions for heat denaturing the sample, allowing the primer to anneal and the reagents/conditions for primer extension (DNA polymerase, dNTPs, etc.) are optimized using standard techniques known to those of skill in the art. **FIG. 12** illustrates transcription of the K-ras DNA target, having 3 point mutations, by the biotinylated primer. A spin column method may be used for simultaneously removing unincorporated biotinylated primer, concentrating the sample, and dialyzing the same into hybridization buffer. --

Please replace the paragraph starting on page 58, line 8 with the following rewritten paragraph:

-- Once immobilized, the target nucleic acid is then detected using a probe that hybridizes to a portion of the target nucleic acid sequence. Specific probes and conditions for hybridizing generic sequence tagged probes to the immobilized target are developed, see U.S. Application Serial No. 09/846430 by Lai et al. entitled "Methods and Compositions for Polynucleotide Analysis using Generic Capture Sequences", filed on April 30, 2001 and incorporated by reference for all purposes. For instance, in the case of K-ras nucleic acid, normal allele-specific oligonucleotide (ASP) probes are tested. Alternatively, the loop probe oligonucleotide may be used, as described in U.S. Patent No. 6,500,622 by Bruchez et al. entitled "Methods of Semiconductor Nanocrystals in Bead-Based Nucleic Acid Assays", filed on March 22, 2001 and incorporated by reference herein for all purposes. As shown in **FIG. 15**, the captured strands are probed using sequence-tagged hybridization probes. Conditions are then applied that are sufficiently stringent to remove non-specifically bound probe. --